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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/962,560	10/31/97	HILTON	D 10976

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EXAMINER	
SRIVASTAVA,D	
ART UNIT	**PAPER NUMBER**
1653	15

DATE MAILED: 02/24/00

Please find below and/or attached an Office communication concerning this application or pr ceeding.

Commissioner of Patents and Trad marks

Office Action Summary

Application No.	Applicant(s)
08/962,560	Hilton et al.
Examiner	**Group Art Unit**
Devesh Srivastava, Ph.D.	1653

☒ Responsive to communication(s) filed on *Jan 6, 2000*

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claim

☒ Claim(s) *1-40* is/are pending in the applicat

Of the above, claim(s) *16-40* is/are withdrawn from consideration

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-5 and 13-15* is/are rejected.

☒ Claim(s) *6-12* is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☒ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☑ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☒ All ☐ Some* ☒ None of the CERTIFIED copies of the priority documents have been

☒ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). *6*

☐ Interview Summary, PTO-413

☒ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

— SEE OFFICE ACTION ON THE FOLLOWING PAGES —

DETAILED ACTION

Response to Restriction Requirment

1. Applicant's election with traverse of Group I, claims 1-15 as related to mouse SOCS species and represented by SEQ ID NO:3 and nucleic acid sequence SEQ ID NO:4, in Paper No. 14 is acknowledged. The traversal is on the ground(s) that (1) the groups of claims are not "independent and distinct" and (2) that issues of double patenting may arise in divisional applications. This is not found persuasive because the restriction requirement set forth in Paper No. 12 establishes ways in which the inventions are related, and therefore found in a single application, and ways in which they are distinct and therefore implicitly independent of each other. The independent nature of the inventions comes from the fact that, for example, the nucleic acids of invention I can be used for a process other than the production of the polypeptide of Invention II. In other words, since the inventions are distinct for the reasons of record, they are also independent. Further, the serious burden of search has already been established for the groups, please see page 5, last two paragraphs, of the previous Office Action. Issues of obvious-type double patently would only arise in cases where Applicant pursues subject matter previously elected in a parent case. A rejection of obvious-type double patenting serves to prevent extension of patent term but would not prevent Applicant from pursuing a different scope of claims in a child case.

The requirement is still deemed proper and is therefore made FINAL.

Specification

2. The disclosure is objected to because of the following informalities: The Brief Description of the Drawings does not have a separate description for Figure 17, the description of Figure 19, at page 24, line 15, Figure 22, at page 25, line 7, Figure 25, at page 25, line 29, Figure 28, at page 26, line 20, Figure 30, at page 27, line 5, Figure 33, at page 27, line 23, Figure 37, at page 28, line 22, Figure 38, at page 28, lines 30-31, Figure 41, at page 29, line 23, Figure 44, at page 30, line 13, and Figure 46, at page 31, line 1, omits information pertinent to the figure. It is recommended to use words to define figure symbols and/or shading since the specification is limited to text or chemical and mathematical formulae and tables (please see text of 37 CFR 1.58(a) below).

37 CFR §1.58 Chemical and mathematical formulae and tables.

(a) The specification, including the claims, may contain chemical and mathematical formulas, but shall not contain drawings or flow diagrams. The description portion of the specification may contain tables; claims may contain tables either if necessary to conform to 35 U.S.C. 112 or if otherwise found to be desirable.

Appropriate correction is required.

Claim Objections

3. Claims 6-12 are objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim cannot depend from any other multiple dependent claim. See MPEP § 608.01(n). Claim 6 is drawn to any one of claims 1-5, however, claim 4 is already drawn to either of claim 2 or 3. Accordingly, the claims (Claims 6-12) have not been further treated on the merits.

Claim Rejections - 35 USC § 101

4. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

5. Claims 1-6 and 13-15 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. Amendment to the claims to recite an isolated nucleic acid molecule would obviate this rejection.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 1-5 and 13-15 are rejected under 35 U.S.C. 112, **second paragraph**, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

8. Claim 1 is drawn to a nucleic acid molecule comprising a[n unspecified] "*sequence*" of nucleotides that encode or are complementary to a[n unspecified] "*sequence*" encoding a protein that comprises a SOCS box in its C-terminal domain. The structure (nucleic acid and amino acid sequence) of the unspecified sequences to which the claim is drawn is unclear. Without a clear identification of these unspecified sequences, it is not possible to define the metes and bounds of the patent protection desired. Claims 2-5 are included in this rejection because they are dependent on rejected claims and do not correct the deficiencies of the claim from which they depend.

9. Claims 1 and 15 recite the limitation "*complementary*", however, it is unclear if the degree of complementarity is to the full or partial sequence. Claims 2-5 are included in this rejection

because they are dependent on rejected claims and do not correct the deficiencies of the claim from which they depend.

10. Claims 1 and 15 recite the limitations "*a derivative, homologue, analogue or mimetic thereof*", however, it is unclear what structural and functional limitations define a derivative, homologue, analogue or mimetic thereof. Further, it is unclear if the "derivative, homologue, analogue or mimetic" refers to the encoded protein or the sequence of nucleotides. Without a clear definition of these terms and what they relate to, it is not possible to define the metes and bounds of the patent protection desired. Claims 2-5 are included in this rejection because they are dependent on rejected claims and do not correct the deficiencies of the claim from which they depend.

11. Claims 1 and 13-15 recite the limitation of "*a nucleotide sequence capable of hybridizing thereto under low stringency conditions at 42°C*", however, the claim fails to identify the equally important wash conditions as well as the salt concentration of the hybridization and wash buffers. Factors to be considered in hybridization procedures include the composition of the hybridization and wash solutions, the temperature of hybridization and wash conditions, and the salt concentration for hybridization and wash solutions. Most of these essential components for hybridization are not clearly specified and thereby render the claims indefinite because the resulting claims do not clearly set forth the metes and bounds of the patent protection desired. Without such guidance, one skilled in the art would not know when he/she would be infringing on Applicant's patent. Therefore, the claims are vague and indefinite. Claims 2-5 are included in

this rejection because they are dependent on rejected claims and do not correct the deficiencies of the claim from which they depend.

12. Claims 2, 3, 5 and 15 recite the limitation wherein the encoded protein further comprises a "*protein:molecule interacting region*" and claim 4 recites the limitation wherein the encoded protein further comprises a "*protein:DNA binding region*" or a "*protein:protein binding region*". Claims 2-5 are dependent on claim 1, which is drawn to a nucleic acid molecule comprising a sequence of nucleotides encoding a protein comprising a SOCS box in its C-terminal region. Claim 15 is also drawn to a nucleic acid molecule comprising a sequence of nucleotides. Since the nucleic acid molecules of claims 1 and 15 are drawn to a "sequence", it is unclear what the structure of these interacting regions comprise.

13. Claims 13 and 14 recite the limitation "*substantially set forth in*", however, it is unclear what makes a nucleotide sequence "substantially" the same as a specified sequence.

14. Claims 13 and 14 recite the limitation "*having*", however, it is unclear if Applicants intend the term to mean "consisting of" or "comprising".

15. Claims 13 and 14 are directed to a nucleic (claim 13) or an encoded amino acid (claim 14) sequence "*having at least 15% similarity to all or part of the listed sequences*". It is unclear what properties, on the nucleic acid or amino acid level, defines a polynucleotide or polypeptide as being similar to the reference sequence. For example, it is unclear if similarity encompasses only conservative amino acid substitution or does it also include silent substitutions that do not result in functional changes in the encoded protein. Without such guidance, one skilled in the art

would not know when he/she would be infringing on Applicant's patent. Therefore, the claims are vague and indefinite.

16. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

17. Claims 1-5 and 13-14 are rejected under 35 U.S.C. 112, **first paragraph**, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claims 2-5 are included in this rejection because they are dependent on rejected claims and do not correct the deficiencies of the claim from which they depend.

Claims 1 and 13-14 are directed to all possible nucleic acid molecules capable of hybridizing to a reference nucleic acid sequence (claims 1, 13 and 14). The specification, however, only provides the species listed in Table I that are encompassed by these claims. There is no disclosure of any particular structure to function/activity relationship in the disclosed species. In fact, Hilton et al. teach that "*The SOCS proteins share structural similarities...To date, however, the role of each part of the protein in inhibiting signal transduction is far from clear, although regions in addition to the SH2 domain appear to be required.*" (*Proc. Natl. Acad. Sci. USA* 95:114-119, Jan., 1998, see especially page 114, right column, first paragraph). Without guidance for structure to function/activity, one skilled in the art would not know which portions of the sequence (structure) are essential for function/activity to produce a functional

polypeptide. Given the lack of a structure to function/activity relationship as encompassed by the claims, Applicants have failed to sufficiently describe the claimed invention, in such full, clear, concise, and exact terms that a skilled artisan would not recognize Applicants were in possession of the claimed invention.

18. Claims 1-5 are rejected under 35 U.S.C. 112, **first paragraph**, because the specification, while being enabling for specific nucleic acid molecules listed in Table 1 of the specification, does not reasonably provide enablement for all nucleic acid molecules *"comprising a sequence of nucleotides encoding or complementary to a sequence encoding a protein or a derivative, homologue, analogue or mimetic thereof or a nucleotide sequence capable of hybridizing thereto under low stringency conditions...wherein said protein comprises a SOCS box in its C-terminal region*". The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in In re Wands (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). The factors most relevant to this rejection are the scope of the claims, unpredictability in the art, the amount of direction or guidance presented, and the amount of experimentation necessary.

The claims are drawn to encompass all nucleic acid molecules *"comprising a sequence of nucleotides encoding or complementary to a sequence encoding a protein or a derivative, homologue, analogue or mimetic thereof or a nucleotide sequence capable of hybridizing thereto under low stringency conditions...wherein said protein comprises a SOCS box in its C-terminal*

region". The specification, however, only discloses the full length sequences of a polynucleotide encoding a SOCS box protein from mouse, human and rat (see Table 1 for listing of those sequences). There is no disclosure or description of any other nucleic acid molecules that encompass the full scope of the claims, including those that encode derivatives, homologues, analogues or mimetics thereof. Further, there is no guidance to how one skilled in the art would construct such a nucleic acid molecule, especially without a sequence from which to begin construction. Despite knowledge in the art for the production synthesis or isolation of of polynucleotides, the claims encompass enormous numbers of polynucleotides for which the structures are unknown. Thus the claims are directed to specifically encompass enormous numbers of embodiments expected to be inoperative. Since it is not routine in the art to engage in *de novo* experimentation to make polynucleotides that encode a protein having SOCS activity where the expectation of success is unpredictable, the skilled artisan would require additional guidance in order to make and use polynucleotides in a manner reasonably commensurate with the scope of the claims. Without such guidance, the experimentation left to those skilled in the art is undue.

19. Claims 13 and 14 are rejected under 35 U.S.C. 112, **first paragraph**, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention (emphasis added).

Factors to be considered in determining whether undue experimentation is required, are summarized in In re Wands (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). The

factors most relevant to this rejection are the scope of the claims, unpredictability in the art, the amount of direction or guidance presented, and the amount of experimentation necessary.

The claims are drawn to encompass all polynucleotides that are at least about 15% similar to all or part of an amino acid sequence of SEQ ID NO:4 (claim 13) or at least about 15% similar to all or part of a nucleic acid sequence of SEQ ID NO:3 (claim 14). The specification, however, only discloses the nucleic acid sequence set forth in SEQ ID NO:3 and the amino acid sequence of SEQ ID NO:4. There is no disclosure or description of even a single example of a polynucleotide that is 15% similar to all or part of SEQ ID NO:3 and that has SOCS activity, which is Applicants' invention. Despite knowledge in the art for the production of polynucleotides encoding a protein with an activity such as the instant invention, the claims encompass enormous numbers of polynucleotides altered to such an extent so that it would not be expected by the skilled artisan to encode SOCS activity (see items 17 and 20 for discussion of issues related to art teachings directed to lack of enablement due to an absence of structure to function relationship in SOCS proteins). Thus the claims are directed to specifically encompass enormous numbers of embodiments expected to be inoperative. Applicants have not taught how to use this enormous number of inoperative embodiments and the effort to identify those embodiments that are functional amounts to undue experimentation. The number of embodiments for an amino acid that is 15% identical to the amino acid sequence set forth in SEQ ID NO:4 is greater than 10^{307} (see sample of method to estimate the number of potential embodiments attached at the end of this Office Action as well as results from an Excel spreadsheet calculation to determine this value). In fact, Excel is incapable of calculating the actual value since the upper limit for a

numerical value in Excel is 10^{307}. Clearly, this enormous number of embodiments that include large numbers of inoperative embodiments amounts to undue experimentation. Since it is not routine in the art to engage in *de novo* experimentation to make polynucleotides that are 15% identical to a reference sequence and encode SOCS activity where the expectation of success is unpredictable, the skilled artisan would require additional guidance in order to use polynucleotides in a manner reasonably commensurate with the scope of the claims. Without such guidance, the experimentation left to those skilled in the art is undue.

20. Claims 1-5 and 15 are rejected under 35 U.S.C. 112, **first paragraph**, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Claims 2-5 are included in this rejection because they are dependent on rejected claims and do not correct the deficiencies of the claim from which they depend.

Factors to be considered in determining whether undue experimentation is required, are summarized in In re Wands (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). The factors most relevant to this rejection are unpredictability in the art, the amount of direction or guidance presented, and the amount of experimentation necessary.

Claims 1-5 are directed to a nucleic acid molecule comprising an unspecified sequence of nucleotides that encode a SOCS protein. Claim 15 is drawn to polynucleotides comprising a sequence of nucleotides encoding a SOCS box in its C-terminal region wherein the SOCS box comprises an amino acid sequence charted in claim 15, item (I), encodes at least one SH2 domain, WD-40 repeats and/or ankyrin repeats and modulates signal transduction (see claim 15 in its

entirety). The specification, however, only discloses the species outlined in Table 1. The art teaches that "*The SOCS proteins share structural similarities. Each has an N-terminal region of variable length and highly variable amino acid sequence, a central SH2 domain, and a striking region of C-terminal homology that we designated the SOCS box (4). Given the sequence similarity evident in the SOCS box of the four SOCS proteins and its conserved position at the C terminus of each protein, it seems likely that this domain has a conserved and important function.* ***To date, however, the role of each part of the protein in inhibiting signal transduction is far from clear, although regions in addition to the SH2 domain appear to be required*** [emphasis added] *(5).*" (*Proc. Natl. Acad. Sci. USA* 95:114-119, Jan., 1998, see especially page 114, right column, first paragraph). In essence, the art, which comes from Inventors Hilton, Richardson, Alexander, Viney, Willson, Starr, Nicholson, Metcalf and Nicola, teaches that a structure to function relationship critical for SOCS proteins to modulate signal transduction was not known in 1998, which is after Applicants' filing of the instant application. Thus the claims are directed to specifically encompass enormous numbers of embodiments expected to be inoperative. Since it is <u>not</u> routine in the art to engage in *de novo* experimentation to make polynucleotides that encode SOCS proteins where the expectation of success is unpredictable, the skilled artisan would require additional guidance in order to make and use such polynucleotides. Without such guidance, the experimentation left to those skilled in the art is undue.

Claim Rejections - 35 USC § 102

21. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

22. Claims 13 and 14 are rejected under 35 U.S.C. 102(b) as being anticipated by Watson et al. (Molecular Biology of the Gene, 4th edition). This rejection is directed to that portion of the claim that recites "*having at least 15% similarity to all or part of the listed sequences*" (emphasis added).

Watson et al. teach nucleic acids encoding individual amino acids (see table from inside cover of text). For example, the codon CUU encodes leucine. Therefore, Watson et al. teach an isolated nucleic acid molecule that encodes a protein having at least 15% similarity to a part of the nucleic acid sequence of SEQ ID NO:3 (claim 14) and to a part of the amino acid sequence of SEQ ID NO:4 (claim 13). Thus, Watson et al. anticipate the claims.

23. Claim 13 is rejected under 35 U.S.C. 102(e) as being anticipated by Smith et al. (US Patent 5,871,960). This rejection is directed to that portion of the claim that recites "*having at least 15% similarity to all or part of the listed sequences*".

Smith et al. teach a nucleic acid sequence, SEQ ID NO:9, that has 45% sequence similarity to a nucleic acid encoding Applicants' instant SEQ ID NO:4 (see attached results of a

sequence search wherein instant SEQ ID NO:4, appearing as three letter amino acid abbreviations, shares 45% similarity with the instant SEQ ID NO:4). Therefore, Smith et al. anticipate the claim.

24. Claim 14 is rejected under 35 U.S.C. 102(b) as being anticipated by Schaffer et al. (WO94/28156, Dec. 8, 1994). This rejection is directed to that portion of the claim that recites "*having at least 15% similarity to all or part of the listed sequences*".

Schaffer et al. teach a nucleic acid sequence, designated as accession number Q76213, that shares 46% best local similarity with Applicants' instant SEQ ID NO:3 (see attached Result 14 of a sequence search wherein instant SEQ ID NO:3 was used as the query term, designated Qy, against the N_Geneseq_36 database). Therefore, Schaffer et al. anticipate the claim.

Conclusion

25. Claims 1-5 and 13-15 are rejected.

26. Claims 6-12 are objected to and have not been further examined on their merits.

27. Claims 16-40 are withdrawn from further consideration for being drawn to non-elected inventions.

28. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Devesh Srivastava, Ph.D. whose telephone number is (703) 305-0775. The examiner can normally be reached on Monday-Thursday from 8:00 am to 5:30 pm and alternate Fridays from 8:00 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low, Ph.D., can be reached on (703) 308-2923. The FAX phone number for the Art

Unit where this application or proceeding is assigned is (703) 308-0294. For direct submission of official papers, by facsimile, with the Patent Office, the FAX phone number is (703) 308-4242 or (703) 308-2742.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Devesh Srivastava, Ph.D.
Patent Examiner
February 16, 2000

Karen Cochrane Carlson PhD

KAREN COCHRANE CARLSON, PH.D
PRIMARY EXAMINER